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THE RELATION BETWEEN TROPHIC LESIONS AND DISEASES OF THE NERVOUS SYSTEM.[1]

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THE question chosen by the council of the Association for discussion to-day, viz.: "*The relation between trophic lesions and diseases of the nervous system, excluding changes within the central nervous system itself,*" is one which brings the critic face to face with an enormous accumulation of more or less well-observed, widely diverse, and not necessarily correlated clinical and experimental facts or data.

The very terms of the question involve to my mind a petitio principii: for the essential query in any review of the data is whether the lesions referred to are really trophic, in nervous causal relation.

Your referee has been informed that "permanent vaso-motor changes, in so far as they can be shown to influence nutrition," may or should be included in the discussion. This I consider a wholly different field of physio-pathology and one whose introduction into the discussion would only tend to obscure, complicate and indefinitely extend the search after the true relation between trophic lesions and nervous diseases; and I shall consequently omit it from my remarks.

[1] Referee's paper read before a joint meeting of the Association of American Physicians and the American Physiological Association during the Congress of American Physicians and Surgeons at Washington, D. C., Sept. 20, 1888.

We must also insist upon a strict definition of the word lesion, as meaning a positive histological alteration in tissue, thus excluding retarded or imperfect development, simple quantitative reduction of tissues, and alterations in local circulation and calorification (as observed in cerebral and spinal paralyses occurring before the full growth of the body, and occasionally after it).

Thus simplified the question may be re-stated in the following terms:

What are the lesions which may be supposed to be directly produced by disease of the nervous system (brain, spinal cord, and nerves); and what is the essential causal relation between the two factors?

To attempt to enumerate separately in a systematic manner all the lesions of the non-nervous tissues which have been observed clinically and experimentally, and ascribed to a direct morbid nervous influence (positive or negative), would be an extensive work, far beyond the time limits of this discussion.

Such "trophic lesions" have been described as occurring in almost all the non-nervous organs and tissues, internal and external. We find medical literature filled with examples of such lesions in the cutaneous tissue and appendages, in the muscular tissue, in bones and articulations, in vascular walls, in parenchymatous organs, and in internal epithelial structures. In other words, wherever nerve fibres terminate, and even where none can be demonstrated (as in cartilage) such lesions have been described.

Some simple mode of classification of these data must be chosen to facilitate discussion, and looking at the subject from the standpoint of the pathologist and practical physician I would suggest the following:

FIRST CLASS.—"Trophic lesions" occurring in parts whose sensibility is more or less reduced by the nervous disease, and which are exposed to the action of traumatic and infectious influences.

This class includes by far the largest number of the data, such as cutaneous ulcerations, fall of nails and hair, altered appearance of skin and nails, articular changes (arthropa-

thies), fractures of bones, deep eschars, necrosis of digits, and most of the lesions observed in the hollow viscera lined by epithelia. To put it in another way, this class includes the various lesions observed in the course of posterior spinal sclerosis, injuries of the spinal cord, forms of "myelitis" so-called, and injuries to nerve-trunks. Speaking before this audience it is useless to further specify the "trophic lesions" referred to.

SECOND CLASS.—Trophic lesions occurring in deeper parts, not exposed to bacterial infection, and upon which traumatic influences cannot be demonstrated to act: in other words, the apparently spontaneous trophic lesions. This class is made up of the muscular atrophies occurring in the course of nervous diseases, and of a limited number of cutaneous lesions. Possibly some alterations in glandular function, due to nerve lesion, may belong to this class. Clinically these lesions are met with after nerve section, in the course of neuritis, and of disease affecting primarily or at least chiefly the ventral cornua of the spinal cord and their homologues in the cephalic prolongation of the spinal axis.

With respect to the first class of so-called trophic lesions, a careful study of the conditions under which they arise, and a comparison of them with the similar peripheral lesions which present as complications at the close of some non-nervous diseases with tendencies to asthenia and inanition, make it somewhat doubtful whether they can rightly be considered as direct results of suppressed or perverted nervous action. Even the strongest partisan of the truly dystrophic nature of these lesions admits that extraneous influences (as trauma and bacterial infection) play a certain though wholly secondary part in their genesis. But other observers hold an opposite extreme view, and claim that the real or efficient causes of the lesions are trauma and infection acting upon parts which have lost their automatic defence through anæsthesia, and whose circulation and general nutrition are lowered, but not specifically altered, by disease and inertia.

This second view is, I must say, supported by negative

evidence, experimental and clinical, of such importance that it needs to be stated.

(*a.*) Ulceration of the cornea and even panophthalmitis are results of experimental and pathological injury to the trigeminus nerve, more especially of its ophthalmic branch and of the Gasserian ganglion. These ocular lesions are fully described in text-books, and are generally looked upon as typical trophic changes due to the nerve disease. Yet thirty years ago H. Snellen[1] and M. Schiff[2] separately demonstrated by the simple experiment of sealing the eye by sewing the edges of the lids or by fastening one of the animal's ears over it, that ulceration of the cornea could be prevented after section of the trigeminus. At some time prior to 1872 von Gudden[3] proved the same thing by a beautiful experiment. He took newly-born rabbits and produced perfect closure of the eyelids by an operation (artificial ankyloblepharon). When the wounds were healed, and the eyes absolutely sealed, he cut the trigeminus nerve by the usual intra-cranial method. Upon opening the eyelids from eight to fifteen days after the nerve-section he invariably found the cornea normal. These experiments make it clear that the nerve lesion is not the real or efficient cause of the corneal changes in the usual experiments, and probably not in human cases of disease of the fifth nerve.

(*b.*) Section and other injuries of nerve-trunks have long been known to be followed by so-called trophic lesions in the distal parts supplied by the injured nerve. Changes in the skin and hairs, falling of the nails, ulceration, and even extensive necrosis or gangrene have been elaborately described in animals and in man. Yet it is nearly forty years since Brown-Séquard[4] showed that (in animals) if the parts

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[1] H. Snellen, De invloed der zennwen, op. de onsteking. Dissert. Utrecht, 1857. Also in Archiv. f. d. Hollandische Beitrage zur Natur. Heilkunde, Bd. I. 3, p 206 (1857).

[2] M. Schiff, in Canstatt's Jahresbericht, I., p, 121, 1857.

[3] Von Gudden, cited by Kondracki in his thesis, Ueber die Durchschneidung des Nervus Trigeminus, Zurich, 1872.

[4] Brown-Sequard, Gazette Medicale, 1849, p. 880.

supplied by the injured nerve be kept perfectly clean and protected from traumatic influences, ulcerations, etc., did not ensue. He also demonstrated that wounds made in parts supplied by an injured nerve-trunk healed as well as wounds made elsewhere. These experiments (confirmed by numerous observers) show that the nerve injury in such experiments or cases is not the true efficient cause of the ulcerations, etc., and also (what is fully as important) that the nutritive functions which go to repair wounds are fully active in anæsthetic and paralyzed parts. In the practice of medicine we have frequent occasion to apply these data, in the prevention and treatment of ulceration, bed-sores, etc., by mechanical and antiseptic measures, after injuries to nerves or to the spinal cord, as well as in cases of paraplegia. In human cases of section of sensory nerves, while certain quantitative changes in the anæsthetic area are apparently inevitable, actual histological lesions can, I believe, be indefinitely prevented by guarding against traumatic influences.[1] As regards bed-sores in paraplegia you have probaby all seen them show healthy reparative action while the spinal disease was growing worse.

(*c.*) It is a remarkable fact that such lesions as perforating ulcer, arthropathies, fractures, etc., which occur in the course of posterior spinal sclerosis and other nervous affections, are extremely rare in patients whose circumstances enable them to avoid over-exertion in the later stages of the disease, and to receive every needed care. This certainly would point to traumatism as a potent factor in the production of the so-called trophic lesions of tabes.

(*d.*) Cystitis was until a comparatively recent time considered one of the symptoms of myelitis and of injury to the spinal cord; though I suppose most of us to-day would speak of it as a complication preventable by the use of aseptic catheters introduced with the greatest care.

The negative demonstrations and arguments to the effect

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[1] Except some lesions of the second class which are unpreventable, though it would seem not invariable results of nerve injuries.

that the greatest number of the most formidable of the so-called trophic lesions of the first class are preventable and curable, appear to my mind almost overwhelming proof that the efficient cause of these lesions is not a suppression or perversion of nervous action or influence.

Consequently I would refuse the name of trophic lesions to the phenomena embraced in the first class of data.

We are now brought to the study of the second class of "trophic lesions," those in which extraneous or traumatic causes cannot be shown to act. It is perhaps in the study of these that the problem of the relation between the nervous disease and the lesion can be best approached.

The most typical lesions of the second class are muscular atrophy with degeneration, and the cutaneous affection known as herpes or zona. Probably other so-called skin diseases belong to this group, but full demonstration of their nervous origin is wanting.

(*a.*) The natural history of neuro-muscular atrophic degeneration is well known to all of you. Within a few days after section of a nerve-trunk, or after destruction of the ventral ganglion cells with which a nerve-trunk is associated in the spinal axis (clinically, in cases of nerve injury, neuritis, poliomyelitis, chronic degeneration of ventral ganglion cells, etc.), the nerve fibres distal of the point of injury or disease, and all the muscles innervated by the fibres lose certain properties known as conductibility and irritability, react abnormally to electrical stimulation, and if examined with the microscope show distinct and invariable alterations. Later, the affected muscles undergo a marked reduction of volume.

In adult animals, after certain lesions, an extreme degree of atrophy is established and persists. In young animals, after certain lesions (simple nerve injuries and neuritis more especially), a process of regeneration sets in which in a few months leads to return of a normal anatomical state of the nerves and muscles, and to renewed functional activity. In some cases there are also more diffused changes produced, arrest of development of parts, quantitative modifications which should not be confounded with actual lesions. What

I wish to emphasize is that we have here to deal with *qualitative or histological changes in nerves and muscles, which occur with fatal necessity when the cause has acted,* and which are demonstrable by microscopic examination and by electrical tests (reaction of degeneration). Further, that these lesions are unpreventable, and in one sense incurable; no traumatic or infectious influence can be traced in their genesis, and no amount of care or any form of treatment will prevent the appearance or thwart the evolution of the changes.

(*b.*) The so-called herpetic lesions of the skin. The vesiculo-pustular affection appears all at once or in successive crops upon areas of skin supplied by one or more of the cerebro-spinal nerves; the distribution of the primary eruption and of the subsequent scars corresponding exactly with nerve territories. Hence the names for varieties of herpes, such as H. frontalis, H. corneæ, H. progenitalis, H. intercostalis, etc., etc. Along with the eruption there are not rarely subjective symptoms of nerve irritation, such as burning, prickling, pain, or numbness. In some cases pain (neuralgia) persists long after the eruption has subsided. Usually, scars remain, and they may be extremely deep. Autopsies have shown, beyond room for doubt, that in such cases the nerve trunk supplying the affected cutaneous area, and especially the ganglion upon its dorsal root, are the seat of inflammatory and degenerative processes. Unfortunately, with the means at our command the lesion has not yet been traced into the terminal filaments and end-organs of the affected nerve in the cutis and epidermis. The demonstration is, however, almost complete that we are here in presence of a neuro-cutaneous and continuous lesion, corresponding to the continuous lesion observed in (*a.*) the neuro-muscular apparatus. Here again we have to deal with an evidently non-traumatic and non-infectious lesion (the skin lesion), revealed by regular and constant symptoms, unpreventable by mechanical means and incurable in a strict sense of the word.

Similar herpetic cutaneous lesions are observed after injuries, more especially such as give rise to irritative and

inflammatory conditions of the nerves. Simple section is more apt to be followed only by cutaneous alterations of the first class. It is, furthermore, possible that traumatic neuritis may produce other true lesions of the skin besides herpes, but this is not yet proven.

To these two varieties of lesions, embraced in the second of the classes which I propose, I am ready and willing to apply the term *trophic lesions* in the true sense of the word; *i. e.*, they are *histological alterations set up directly and fatally by the nerve disease, without the intervention of accidental or extraneous causes.* The relation of cause and effect seems indisputable, and we may therefore say that the efficient cause of the trophic lesion is disease of a part of the nervous system.

And, now, as to the mechanism or physiology of these trophic lesions. We cannot go far in this direction without entering the domain of pure speculation. It is only a few weeks since I heard my illustrious master and friend, Professor Charcot, state in a clinical lecture that we know absolutely nothing of trophic nerves and their mode of action. In this negation I most fully concur, especially if it be applied to the confused or unclassified mass of so-called trophic lesions about which so much has been written. The existence of trophic nerves as such is unanimously denied by physiologists, and much of the speculations of physicians have been made without scientific basis in anatomy and physiology.

The attempt to simplify the problem which I herewith submit to the Association may not advance our actual knowledge, but it may possibly serve as a step toward a more exact study of the subject, and may give rise to a beneficial discussion. Allow me in closing to attempt to show in what way this analysis may be a slight step in advance.

I have, in the first place, rejected from the category of trophic lesions all vaso-motor, calorific, and metabolic phenomena, as well as all mere quantitative reductions in tissues and organs; reserving the name for such alterations as are characterized by demonstrable histological changes.

This will doubtless be objected to, as in a certain sense the excluded phenomena have much to do with nutrition, and the word "trophic" leads the mind inevitably to think of *changes in nutrition*, which for me is far too vague and general a conception to prove of help in the study of our subject. Besides, since Claude Bernard's, Brown-Séquard's and Ludgwig's discoveries a sort of antagonism has been revealed between mere vaso-motor variations and the activity of the cellular life (salivary secretions, etc.).

In the second place, I have attempted to show that histological lesions apparently due to nervous disease may be divided into two classes; one in which the morbid nervous influence is of doubtful or at least of secondary causal value, while the active or efficient causes of the lesions are extraneous and accidental (traumatism and infection); whereas in the second class (by far the smaller at present) extraneous causes are unimportant or even wholly wanting, while, as far as our present means of observation go, the efficient cause of the lesions is a morbid state of the nervous system.

The phenomena which make up the first class I hold to be mere complications having a complex etiology, while those of the second class are really trophic lesions due to disease of the nervous system.

I would not be understood as claiming that the classification here proposed is final or absolutely exact in all its details. For example, lesions of the second class may co-exist with others of the first class in paralyzed parts: *e. g.*, atrophic or herpetiform lesions in paraplegia of the traumatic form especially. Again, a reasonable doubt may be entertained as to whether arthropathies always belong to the first class of lesions. It would be necessary to make a new analytical study of all varieties of so-called trophic lesions, and classify them according to their histology, etiology, in the light of the subdivision here proposed.

Third.—While not pretending to be able to throw any new light on the intimate nature of real trophic lesions, I desire to point out that possibly (and I say this with all due reserve) the mechanism of these alterations, or as the ques-

tion puts it, the relation between the trophic lesions and disease of the nervous system, lies or is embraced in a law of *inter-dependent life in continuous tissues*. As regards the neuro-muscular changes of our second class, the operation of such a law seems highly probable. Anatomically and physiologically the neuro-muscular apparatus from the ganglion cells of the ventral cornua of the spinal cord to the striated muscular substance is a unity or becomes one before the completion of fœtal life. Whether the ultimate nerve fibrillæ and other prolongations of neural substance which lie under the sarcolemma actually blend with the sarcous substance, is, I know, an unsettled point; but their coaptation and physiological continuity are established. Besides, in lower animal forms true neuro-muscular structures do exist.

With reference to the neuro-cutaneous apparatus, we need still more delicate and reliable histological researches to show what is the true relation between ultimate nerve fibrillæ and the peripheral neural substance with the cells of the cutis and epidermis. While some observers claim actual blending of the two substances, by penetration of nerve fibrillæ into epithelia and by the interposition of cell-like nervous expansions in among the cells of the skin, others are in doubt as to the arrangement. Still, at the present time, the weight of evidence is in favor of the existence of continuity between sensory nerves and some of the elements of the skin. The same statement may be made with reference to the relation existing between the termination of glandular nerves and the epithelia of gland.

I therefore venture to suggest that *disease of the nervous system produces true trophic lesions when it interferes with the associated or inter-dependent life of continuous tissues.*